# PATENT COOPERATION TREATY



# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

| Applicant's or agent's file reference<br>ACR 2994 WO | **FOR FURTHER ACTION** | See Form PCT/IPEA/416 |
|---|---|---|
| International application No.<br>PCT/EP2004/004506 | International filing date *(day/month/year)*<br>28.04.2004 | Priority date *(day/month/year)*<br>29.04.2003 |
| International Patent Classification (IPC) or national classification and IPC<br>B01D9/00 | | |
| Applicant<br>AKZO NOBEL N.V. | | |

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 3 sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

| | | |
|---|---|---|
| ☒ | Box No. I | Basis of the opinion |
| ☐ | Box No. II | Priority |
| ☐ | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| ☐ | Box No. IV | Lack of unity of invention |
| ☒ | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| ☐ | Box No. VI | Certain documents cited |
| ☐ | Box No. VII | Certain defects in the international application |
| ☒ | Box No. VIII | Certain observations on the international application |

| Date of submission of the demand | Date of completion of this report |
|---|---|
| 23.11.2004 | 11.03.2005 |
| Name and mailing address of the international preliminary examining authority:<br>European Patent Office - P.B. 5818 Patentlaan 2<br>NL-2280 HV Rijswijk - Pays Bas<br>Tel. +31 70 340 - 2040 Tx: 31 651 epo nl<br>Fax: +31 70 340 - 3016 | Authorized Officer<br>Hilt, D<br>Telephone No. +31 70 340-4259 |

# INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/004506

## Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

| | |
|---|---|
| **Description, Pages** | |
| 1-31 | as originally filed |
| **Claims, Numbers** | |
| 1-16 | filed with telefax on 23.11.2004 |
| **Drawings, Sheets** | |
| 1/2-2/2 | as originally filed |

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

# INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/004506

## Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Yes: | Claims | 1-12,14-16 |
| | No: | Claims | 13 |
| Inventive step (IS) | Yes: | Claims | |
| | No: | Claims | 1-12,14-16 |
| Industrial applicability (IA) | Yes: | Claims | 1-16 |
| | No: | Claims | |

2. Citations and explanations (Rule 70.7):

**see separate sheet**

## Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

**Re Item V**

**Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Reference is made to the following document:
D1: US-B1-6 221 398 (TROFAST JAN ET AL) 24 April 2001 (2001-04-24)

1. The present application refers to a process for the solidification of inorganic or organic compounds using an antisolvent solidification technique.

2. Claims 1-12

The present application does not meet the requirements of Article 33(1) PCT, because the subject-matter of claims 1-12 does not involve an inventive step in the sense of Article 33(3) PCT.

2.1- Independent method claim 1

Document D1, which is considered to represent the most relevant state of the art, discloses (cf. column 2 line 63 - column 3 line 7; column 4 lines 24-54) a process for the preparation of respirable particles from which the subject-matter of claim 1 differs in that a membrane positioned in a membrane module is used.

Document D1 discloses a process employing a porous filter and in particular a Pyrex Glass Filters of porosity grade 1-4 (pores of 10-160 microns).

Although the examples 1-8 column 5,6 of D1 show a batch type process, the process described in D1 is not limited exclusively to a batch type process. As a matter of fact, it is a normal practice to illustrate a new process with examples made in a laboratory (see examples 1-5 pages 26-31 of the present application). No technical feature limits the process disclosed in document D1 as being exclusively a batch process. So the process of document D1 could be interpreted for the man skilled in the art as being a continuous or a batch process.

The problem to be solved by the present invention may therefore be regarded as to consider others types of porous media.

The solution proposed in claim 1 of the present application cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons:

The use of a membrane as a porous media and its positioning in a membrane module is merely a slight constructional change over the prior art document D1 which the skilled person would select, in accordance to circumstances, without the exercise of inventive skill, in order to solve the problem posed.

2.2- dependent claims 2-12

Dependent claims 2-12 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step.

3- Claims 13-15

3.1- Independent claim 13

The present application does not meet the requirements of Article 33(1) PCT, because the subject-matter of claim 13 is not new in the sense of Article 33(2) PCT.

Claims for products defined in terms of a process are allowable only if the products as such fulfil the requirements for patentability i.e inter alia that they are new and inventive.
A product is not rendered novel merely by the fact that it is produced by means of a new process.
So the passage "obtainable by the process of any one of claims 1-12" has no limiting effect on the scope of claim.

With reference to the clarity problems exposed in Re Item VIII and to the above

comments, the features characterising the crystalline particles of the product claim 13 are:

- comprising at least one pharmaceutical compound
- having a span of the particle size distribution of below 3

With those characterising features, the man skilled in the art can only consider the subject-matter of claim 13 as being not new (Art. 33(2) PCT)

3.2- dependent claims 14,15

Dependent claims 14,15 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step.

4- Claim 16

The subject matter of use claim 16 is characterised only by the use of a process, which is not inventive, to produce a product, which is not new.

So the subject-matter of claim 16 does not involve an inventive step in the sense of Article 33(3) PCT.

**Re Item VIII**

Clarity (Art. 6 PCT)

The term "preferably" used in claim 13 has no limiting effect on the scope of the claim; that is to say, the feature following such an expression is to be regarded as entirely optional, thereby rendering the definition of the subject-matter of said claim unclear,

**INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (SEPARATE SHEET)**

International application No.

PCT/EP2004/004506

Article 6 PCT.

ACR 2994 R

111

**Amended set of claims**

1. Antisolvent solidification process for preparing a solid composition comprising at least one organic or inorganic compound, wherein a liquid medium comprising at least one dissolved organic or inorganic compound is forced through a membrane which is positioned in a membrane module into one or more antisolvents or wherein one or more antisolvents are forced through a membrane which is positioned in a membrane module into a liquid medium comprising at least one organic or inorganic compound, and whereby the process is carried out as a continuous process, yielding a composition comprising solid particles comprising said organic and/or inorganic compound(s).

2. A process according to claim 1 wherein the solidification is a crystallisation, the prepared solid particles are crystalline particles, the organic or inorganic compound is a crystallisable compound, and, optionally, said crystalline particles are recovered from the process.

3. A process according to any one of claims 1-2 wherein the liquid medium is separated from the one or more antisolvents by means of nanofiltration and wherein, optionally, the liquid medium and/or the antisolvent(s) is/are recycled.

4. A process according to any one of claims 1-3 wherein an emulsion is formed before said composition comprising solid particles is obtained.

5. A process according to any one of claims 1-4 wherein a nonsolvent is present in the liquid medium and/or in the one or more antisolvents.

6. A process according to any one of claims 1-5 wherein the organic or inorganic compound is selected from the group consisting of transition metal compounds, transition metal salts, alkali salts, alkali earth salts, fatty acids, proteins, saccharides, aminoacids, and pigments.

7. A process according to any one of claims 1-6 wherein the solid particles essentially consist of particles of only one inorganic or organic compound.

8. A process according to any one of claims 1-7 wherein the inorganic or organic compound is a pharmaceutical compound.

9. A process according to claim 8 wherein the pharmaceutical compound is selected from the group consisting of tibolone, progesterone, desogestrel, and 3-keto-desogestrel (etonogestrel).

10. A process according to any one of claims 1-7 wherein the solid composition comprises a mixture of two or more pharmaceutical compounds.

11. A process according to any one of claims 1-3 wherein a composition comprising solid particles is prepared, in which composition at least part of the particles consists of a core coated with one or more solid coatings of one or more organic or inorganic coating materials, by forcing a liquid medium comprising dissolved organic or inorganic coating material through a membrane into a suspension of particles to be coated in one or more antisolvent(s) for said coating material.

12. A process according to claim 11 wherein the prepared solid composition comprises particles having a core comprising a pharmaceutical compound coated with at least one or more coating materials which comprise a pharmaceutical compound.

13. Crystalline particles obtainable by the process of any one of claims 1-12 comprising at least one pharmaceutical compound which is preferably selected from the group consisting of tibolone, progesterone, desogestrel, and 3-keto-desogestrel (etonogestrel) showing only little and preferably essentially no agglomeration and having a span of the particle size distribution immediately after the crystallisation step of below 3.

14. A pharmaceutical dosage form comprising crystalline particles according to 13.

15. A pharmaceutical dosage form according to claim 14 wherein the dosage form is a tablet.

16. Use of the process according to any one of claims 1-12 or the crystalline particles according to claim 13 in the preparation of a pharmaceutical dosage form.